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Predicting the topology of eukaryotic membrane proteins.

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We show that the so-called 'positive inside' rule, i.e. the observation that positively charged amino acids tend to be more prevalent in cytoplasmic than in extra-cytoplasmic segments in transmembrane proteins [von Heijne, G. (1986) EMBO J. 5, 3021-3027], seems to hold for all polar segments in multi-spanning eukaryotic membrane proteins irrespective of their position in the sequence and hence can be used in conjunction with hydrophobicity analysis to predict their transmembrane topology. Further, as suggested by others, we confirm that the net charge difference across the first transmembrane segment correlates well with its orientation [Hartmann, E., Rapoport, T. A. and Lodish H. F. (1989) Proc. Natl Acad. Sci. USA 86, 5786-5790], and that the overall amino-acid composition of long polar segments can also be used to predict their cytoplasmic or extra-cytoplasmic location [Nakashima, H. and Nishikawa, K. (1992) FEBS Lett. 303, 141-146]. We present an approach to the topology prediction problem for eukaryotic membrane proteins based on a combination of these methods.

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